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Features of severe AECOPD during the influenza a (h₁n₁) epidemic period in 2016-2017

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Abstract

Influenza viruses seemed to be important cause of severe AECOPD. But it is not clear to the end pathogenesis and clinical features of severe AECOPD during seasonal epidemics of flu.

The aim was to study the features of clinical course, severity of lung disorders in patients with severe AECOPD during the 2016–2017 Influenza epidemic and to find possible predictors of lethality during severe AECOPD in this period.

It was a retrospective observational study using medical histories of patients died from severe AECOPD with detected and suspected (according to anamnestic, epimiological and clinical data) Influenza A(H₁N₁), which were hospitalized in intensive care units in epidemic period of 2016–2017.

It was found that patients admitted to the doctor very late, worsening started with febrile and hyperfebrile temperature before hospitalization, great weakness, dry cough; among clinical symptoms acute respiratory failure prevailed; additional symptoms were cachexia and decompensation of cardiovascular comorbidity.

Other features of lethal severe AECOPD were very low parameters of external breathing. According to chest CT-scans most died patients had severe changes of bronchi and lung parenchyma such as chronic bronchitis, lung emphysema, bronchoectasies and bulls. One of the most severe complication was pneumothorax.

The mortality of patients with severe AECOPD depends on too late hospitalization, lack of anti-inflammatory treatment and absence of preventive vaccinations. Severe lung function disorders in anamnesis are the most significant predictor of mortality in patients with COPD during epidemic seasons and should be indicators of early intensive treatment with oxygenation. The key point in the treatment of virus-associated severe AECOPD is early, sufficient and adequate oxygen therapy taking into account the high risk of pneumothoraxes which significantly aggravates the course of disease.

Keywords: AECOPD, Influenza A(H₁N₁), mortality, predictors

1. Introduction

Viral infections of the respiratory tract are the commonest disease syndrome in humans. A number of different viruses can infect the human respiratory tract. Most of them cause self-limiting illnesses such as the common cold or acute bronchitis. The severity of illness depends on the particular virus and on host factors. In patients with airway diseases such as chronic obstructive pulmonary disease (COPD), the morbidity caused by respiratory virus infection is considerably greater. Among respiratory viruses, influenza has the greatest impact in terms of both the morbidity and mortality that it causes. Although influenza affects all age groups, much of the morbidity and mortality are concentrated in high-risk groups such as the elderly and those with concomitant disease, particularly cardiovascular and pulmonary disorders ^[1].

The mortality and utilization of healthcare resources associated with influenza is concentrated in the elderly and those with coexisting disease such as COPD. Increasing use of vaccination and the development of new antiviral drugs hold out hope that the burden of disease associated with influenza can be reduced. However the constant emergence of new influenza strains serve as warnings that influenza will remain a serious pathogen for the foreseeable future ^[1].

Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) cause significant morbidity, mortality, and an inexorable decline of lung function ^[2, 3]. AECOPD can be caused by a number of factors but the commonest cause is infection of the tracheobronchial tree. Historically COPD exacerbations have been considered as being predominantly caused by bacteria, however recent evidence has suggested that respiratory viruses are associated with 40%–60% of COPD exacerbations ^[4]. Data from developed countries have shown viruses to be important causes of severe AECOPD ^[2]. But its pathogenesis and clinical features of severe AECOPD during seasonal epidemics of flu are not quite clear to the end.

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That is why the aim was to study the features of clinical course, severity of lung disorders in patients with severe AECOPD during the 2016–2017 Influenza epidemic and to find possible predictors of lethality during severe AECOPD in this period.

2. Materials and methods

Study design is a retrospective observational study. Materials include medical histories of 35 patients (age from 65 to 75 years old, male – 30 (85,7%)) died from severe AECOPD with detected and suspected (according to anamnestic, epidemiological and clinical data) Influenza A(H₁N₁), which were hospitalized in intensive care units of several city and regional clinics in Dnipro, Ukraine in epidemic period of 2016–2017.

We analyzed results of such methods of investigator as general inspection, pulsoxymetry, spirometry (last data before hospitalization or during hospitalization if possible) with diagnosing of main parameter: forced exhaled volume for the first second after using of bronchodilator (FEV₁ (post)), general and biochemical blood test, microbiological sputum analysis, nasopharyngeal swabs on Influenza A(H₁N₁) (if possible), determination of Influenza A(H₁N₁)-California RNA (if possible).

Statistical processing of the results of research carried out using the methods of biometric analysis, implemented in software packages EXCEL-2003 (№ 74017-641-9475201-57075) and STATISTICA 6.0 (№ 31415926535897) [6].

3. Results and discussion

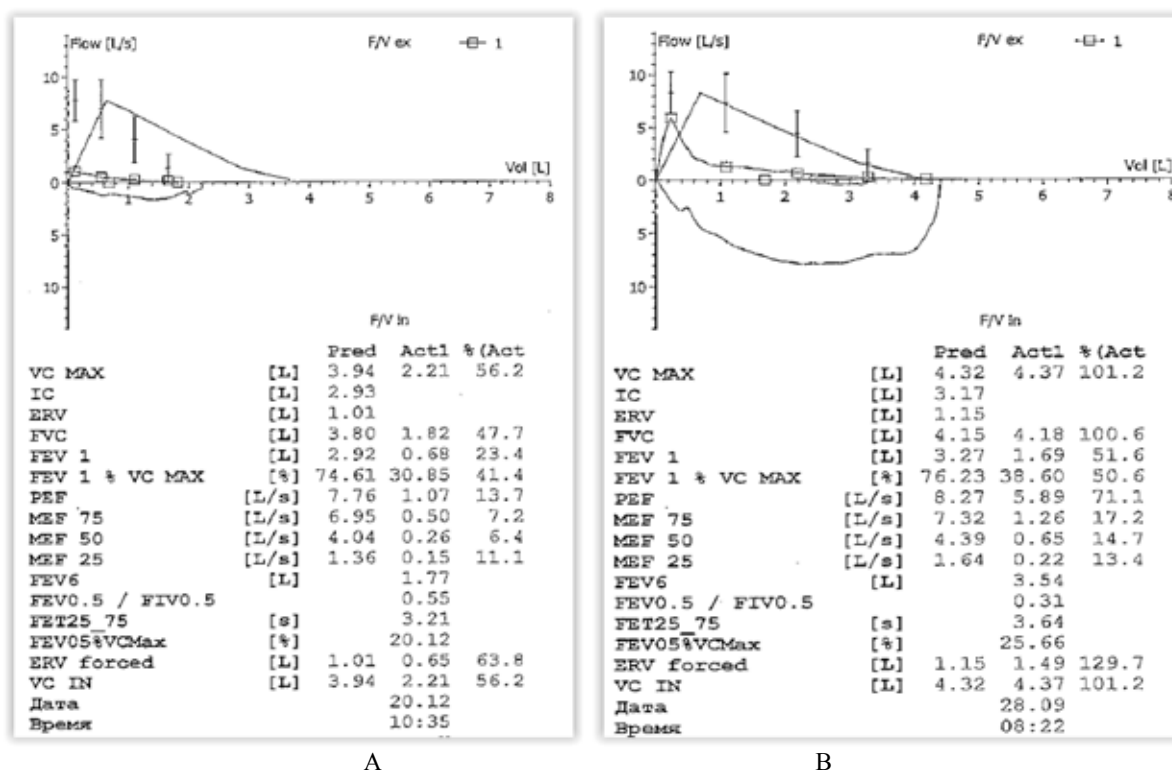
On admission the status of all patients of the group was

reported as serious. After verification of severe AECOPD and the initial survey all patients were assigned to the adequate nebulizer (which included high doses of IGCS in combination with bronchodilators) and antibacterial treatment (which included protected aminopenicillins (amoxicillin/clavulanic acid or ampicillin/sulbactam) or cephalosporins of III generation (ceftriaxone) in combination with macrolides, as an alternative therapy used combination of fluoroquinolones of III or IV generation and "protected" aminopenicillin or cephalosporin of III generation).

During analyzing of anamnesis at died patients with severe AECOPD it was found that patients admitted to the doctor very late. Average length of disease before hospitalization was 5, 6±0,4 days. At most of them (in 32 (91, 4%) patients) this worsening started with febrile and hyperfebrile temperature before hospitalization, great weakness, dry cough.

Among clinical symptoms acute respiratory failure prevailed. It was almost refractory for oxygen therapy (mean saturation was 91, 3±1,9%). Additional symptoms were cachexia (in 32 (91, 4%) cases), decompensation of cardiovascular comorbidity (in 18 (51, 4%) cases).

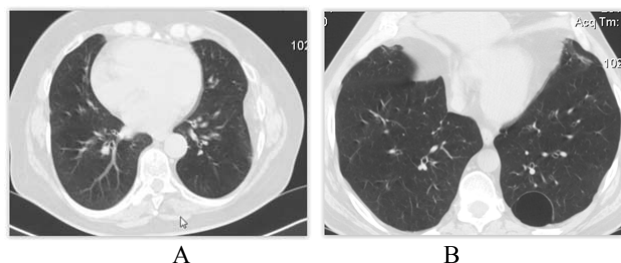
Very low parameters of external breathing were other features of lethal severe AECOPD. According to medical cards it was impossible to do spirometry for these patients in the hospital because of severe state, but from anamnesis and historical documents (if possible) it was known, that average FEV₁(post) was 34,6±1,4% pred. before hospitalization (during 0,5–1 year period), which corresponds to GOLD 3-4. Spirometry with minimal and maximal values are presented on the picture 1A and 1B corresponding.



Picture 1: Historical post-dose spirometric test of patients died from AECOPD with minimal (A) and maximal (B) parameters of FEV₁ (post)

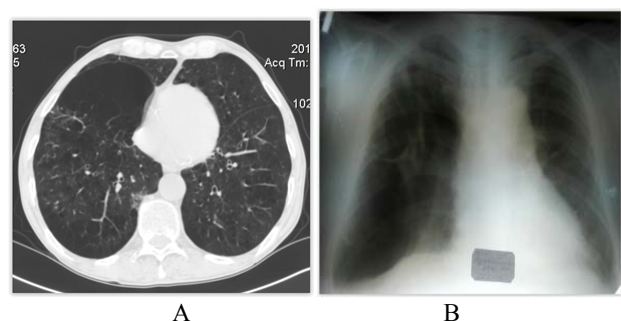
During analyzing if chest CT-scans it was find out that most died patients had severe changes of bronchi and lung parenchyma. Like on presented pictures patients had X-ray

symptoms of chronic bronchitis, lung emphysema, bronchoectasies and bulls (picture 2A and 2B).



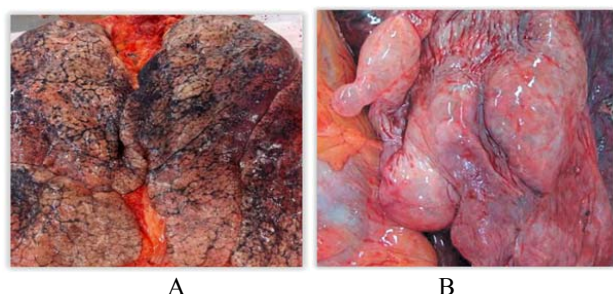
Picture 2: Historical chest CT-scans of patients died from AECOPD: chronic bronchitis, lung emphysema, bronchoectasies (A) and bulls (B)

Pneumothorax was one of the most severe complication, which happened in 17 (56,7%) cases during hospitalization because of severe AECOPD. On picture 3 historical CT-scan slides of the patient died from AECOPD in January 2017 are presented. Patient had giant bull and pneumothorax during staying in the intensive care unit, which aggravated greatly the severity of the patient (picture 3A and 3B).



Picture 3: Historical chest CT-scan (A) with big bull and simple X-ray with pneumothorax (B) of the patient died from AECOPD

On autopsy there were found such pathomorphological signs as hemorrhagic changes on trachea and bronchi, severe lung emphysema with bulls, pneumothoraxes (picture 4A, B).



Picture 4: Lung macropreparation with emphysema (A) and big bulls (B) of the patient died from AECOPD

Microbiological findings were positive only in 5 (14,3%) cases at patients with severe virus-associated AECOPD. Multiresistant *Pseudomonas aeruginosa* (n=2) and multiresistant *Klebsiella pneumoniae* (n=3) were found in sputum and after autopsy in summary.

4. Conclusions

1. The mortality of patients with severe AECOPD depends on too late hospitalization, lack of anti-inflammatory treatment and absence of preventive vaccinations.
2. Severe lung function disorders in anamnesis (FEV_1 (post)

less than 30% pred. and low saturation (less than 95%) are the most significant predictors of mortality in patients with COPD during epidemic seasons and should be indicators of early intensive treatment with oxygenation.

3. The key point in the treatment of virus-associated severe AECOPD is early, sufficient and adequate oxygen therapy taking into account the high risk of pneumothoraxes which significantly aggravates the course of disease.

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